REMARKS

Status of the Claims.

Claims 1-12, 14-17, and 71-73 are pending. Claims 72 and 73 are new. Support for new claim 72 is found in the specification at least at page 11, lines 9-11, taken with page 18, lines 11-13. Support for new claim 73 is found in the specification at least at page 42, lines 15-23. Accordingly, no new matter is added by the amendments.

Substance of the Interview.

Applicants appreciate the courtesy extended to Applicants' Attorney in a telephonic interview with Examiner Alana Harris on May 4, 2009. The outstanding rejections were discussed, and it was agreed that Applicants would not amend the rejected claims, but would re-present previous arguments for the Examiner's reconsideration.

Rejection Under 35 U.S.C. § 112, Second Paragraph.

Claims 1-12, 14-17, and 71 were rejected under 35 U.S.C. § 112, second paragraph, as allegedly indefinite because, according to the Examiner, claims 1 and 9 recite detection steps that are "not commensurate with the target molecule" Office Action, page 5. In particular, the Examiner cites an apparent contradiction between the recitation in claim 1 of "a vitamin D 24 hydroxylase (*CYP24*) gene that can be amplified using amplification primers" and recitations in claims 1 and 9 of detection of an increased level of CYP24 protein. Applicants respectfully point out that claim 1's reference to amplification merely defines the *CYP24* gene as one that can be amplified using the recited primers. In other words, this reference does not limit how one detects the level of CYP24 nucleic acid or CYP24 protein. Withdrawal of the § 112, second paragraph rejection is respectfully requested.

Rejection Under 35 U.S.C. § 112, First Paragraph.

Claims 1-12, 15-17, and 71 were rejected under 35 U.S.C. § 112, first paragraph, as allegedly failing to comply with the written description requirement. Office Action, page 4. This rejection is respectfully traversed.

Claim 1 to recites "a vitamin D 24 hydroxylase (*CYP24*) gene that can be amplified using amplification primers, wherein one primer comprises SEQ ID NO: 1 and another primer comprises SEQ ID NO: 2." Identifying the *CYP24* gene as that which is "amplified using amplification primers, wherein one primer comprises SEQ ID NO: 1 and another primer comprises SEQ ID NO: 2" unambiguously identifies the *CYP24* gene that is the subject of the claimed method.

In support of the rejection, the Examiner notes that the primers would anneal to all *CYP24* genes and thus the "claims continue to encompass a genus of molecules, such as nucleic acids . . . that are not necessarily wild type forms of *CYP24*." Office Action, page 5. The term "wild type" is typically used to refer to a naturally occurring form of a gene, as opposed to one in which mutations have been introduced by a scientist. The claimed method relates to the detection of CYP24 nucleic acid (DNA or mRNA), protein, or activity in a biological sample from a human. The *CYP24* gene in such a sample is the naturally occurring *CYP24* gene, not a gene into which mutations have been introduced by a scientist.

The Examiner goes on to state that "the term reads on a plethora of variant, mutated and alternate forms of *CYP24*." *Id.* It is true that a subject might carry a *CYP24* that has a mutation not found in the majority of the population and that the claims encompass detecting levels of the mutant *CYP24*, as well as the levels of the *CYP24* that is the predominant form. However, despite this fact, one of skill in the art would have no difficulty recognizing that Applicants had possession of methods of detecting the level of CYP24 nucleic acid or CYP24 protein.

First, as Applicants stated in the Amendment filed November 14, 2006:

> A brief Google Scholar search of articles published between 1980 and 1999 identified over 60 published references referring to CYP24 and describing the gene, its structure and regulation in substantial detail . . . . The articles provide clear evidence that the vitamin D 24 hydroxylase (*CYP24*) gene was well known to those of skill in the art and that one of skill in the art clearly understood what is meant by a nucleic acid or protein encoded by the vitamin D 24 hydroxylase (*CYP24*) gene. Moreover, as explained in Applicants'

> previous response, and as evidenced by the publications in Exhibit A [omitted], one skill in the art understood how to measure expression of the CYP24 gene.

Amendment filed November 14, 2006, page 6.

> Second, as stated in the Amendment filed May 29, 2008.
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> [S]ince the claim [claim 1] relates to assaying human samples, the claim relates to the endogenous human gene. The specification cites GenBank Accession No. U60669, which provides the sequence of the "Human 1 alpha, 25-dihydroxyvitamin D3 24-hydroxylase (CYP24) gene," as it is identified in this GenBank record, which includes a sequence that was entered on February 8, 2002, almost 2 months before the priority date of the application. The claim thus requires the detection of protein or nucleic acid corresponding to a known endogenous human gene in a human sample. Applicants were clearly in possession of this invention at the time the application was filed, especially in view of the examples illustrating the detection of DNA, RNA, and protein corresponding to this gene.

Amendment filed May 29, 2008, page 7.

Third, the claims recite that the *CYP24* gene is "a vitamin D 24 hydroxylase (*CYP24*) gene that can be amplified using amplification primers, wherein one primer comprises SEQ ID NO: 1 and another primer comprises SEQ ID NO: 2." All members of this genus share the common feature of appropriate binding sites for the recited primers. This feature distinguishes the *CYP24* gene to be detected from other genes. That members of the genus may differ slightly due, *e.g.*, to allelic variation is of no consequence with respect to the claimed method.

As stated in the M.P.E.P., the "written description requirement for a claimed genus may be satisfied "by disclosure of relevant, identifying characteristics, i.e., structure or other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between function and structure, or by a combination of such identifying characteristics." M.P.E.P., page 2100-182. In addition to the structural characteristics of binding sites for amplification primers comprising SEQ ID NOs:1 and 2, the genus of nucleic acids defined by "a vitamin D 24 hydroxylase (*CYP24*) gene" must encode a 25-hydroxyvitamin D3 24-hydroxylase enzyme. *See* Applicants' specification at page 7, lines 10-12. These two constraints define, with particularity, the structure of

the *CYP24* gene recited in claim 1 and greatly limit the variability between species of *CYP24* genes encompassed by this definition. Accordingly, Applicants submit that the specification meets the M.P.E.P.'s standard for adequate written description of a genus.

The Examiner concluded her written description analysis with the statement that "Applicants have not described *CYP24* with sufficient particularity such that one skilled in the art would recognize that the Applicants had possession of the broad genus of molecules set forth in the claimed invention." Office Action, page 5. Applicants strongly disagree with this position. Applicants actually reduced detection of *CYP24* gene copy number to practice, using the recited primers with four different samples. One of skill in the art would readily appreciate that these primers would amplify all *CYP24* genes that are capable of binding the primers. Accordingly, at the time the application was filed, it would have been possible for Applicants to carry out and describe the amplification of *CYP24* genes from any number of human samples. Each of the amplification products would correspond to the claimed *CYP24* gene. In other words, Applicants could have actually reduced to practice any number of embodiments in which the amplification products contained minor, *e.g.*, allelic, variations *CYP24* gene nucleotide sequences. However, providing additional examples of performing the claimed method with different samples would have added nothing of import to the description. Accordingly, Applicants submit that one of skill in the art would recognize that Applicants were in possession of the invention as of the time the application was filed. Withdrawal of the § 112 rejection for lack of written description is therefore respectfully requested.

Conclusion.

In view of the foregoing, Applicants believe all claims now pending in this application are in condition for allowance. The issuance of a formal Notice of Allowance at an early date is respectfully requested. Should the Examiner seek to maintain the rejections, Applicants request a telephone interview with the Examiner and the Examiner's supervisor.

If a telephone conference would expedite prosecution of this application, the Examiner is invited to telephone the undersigned at (510) 267-4160.

Any required fees accompany this response; if the amount of such fees is incorrect, please charge any required fees, or credit any overpayments, to Deposit Account No. 504480 (Order No. UCOTP089US).

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Respectfully submitted,

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